

### AMENDMENTS TO THE CLAIMS

This listing of claims replaces all previous listing of claims pending in this application.

#### Listing of Claims

1. (Currently amended) A conjugate comprising a  $\beta$ -arrestin protein and a label, ~~detectable molecule~~.
2. (Currently amended) The conjugate of claim 1, wherein said label ~~the detectable molecule~~ is an optically detectable molecule.
3. (Currently amended) The conjugate of claim 1, wherein said label ~~the detectable molecule~~ is Green Fluorescent Protein.
- 4-16. (Cancelled)
17. (Withdrawn – currently amended) A method of assessing G protein coupled receptor (GPCR) pathway activity under test conditions, comprising: a) providing a test cell that expresses a GPCR, and contains a conjugate according to claim 1; ~~comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the test cell to a known GPCR agonist under test conditions; and then c) detecting translocation of said conjugate ~~the detectable molecule~~ from the cytosol of the test cell to the membrane edge of the test cell; wherein the translocation of the detectable molecule in the test cell indicates activation of the GPCR pathway.
18. (Withdrawn) A method according to claim 17 wherein the test condition is the presence in the test cell of a test kinase.
19. (Withdrawn) A method according to claim 17 wherein the test condition is the presence in the test cell of a test G-protein.
20. (Withdrawn) A method according to claim 17 wherein the test condition is exposure of the test cell to a test ligand.
21. (Withdrawn) A method according to claim 17 wherein the test condition is coexpression in the test cell of a second receptor.

Serial No. 10/628,909

Filing Date: July 29, 2003

22. (Withdrawn – currently amended) A method for screening a  $\beta$ -arrestin protein or fragment thereof for the ability to bind to a phosphorylated GPCR, comprising: a) providing a cell that: i) expresses a GPCR; and ii) contains a conjugate according to claim 1; ~~comprising a test  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the cell to a known GPCR agonist; and then c) detecting translocation of said conjugate ~~the detectable molecule~~ from the cytosol of the cell to the membrane edge of the cell; wherein translocation of said conjugate ~~the detectable molecule~~ in the test cell indicates  $\beta$ -arrestin protein binding to the phosphorylated GPCR.

23. (Withdrawn – currently amended) A method for screening a test compound for G protein coupled receptor (GPCR) agonist activity, comprising: a) providing a cell expressing a GPCR and containing a conjugate according to claim 1; ~~comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the cell to the test compound; and then c) detecting translocation of said conjugate ~~the detectable molecule~~ from the cytosol of the cell to the membrane edge of the cell; wherein movement of said conjugate ~~the detectable molecule~~ from the cytosol to the membrane edge of the cell after exposure of the cell to the test compound indicates GPCR agonist activity of the test compound.

24. (Withdrawn) A method according to claim 23 wherein the cell expresses a known GPCR.

25. (Withdrawn) A method according to claim 23 wherein the cell expresses an unknown GPCR.

26. (Withdrawn) A method according to claim 23 wherein the cell expresses an odorant GPCR.

27. (Withdrawn) A method according to claim 23 wherein the cell expresses a  $\beta$ -adrenergic GPCR.

28. (Withdrawn – currently amended) A method according to claim 23 wherein said conjugate ~~the detectable molecule~~ is optically detectable.

29. (Withdrawn – currently amended) A method according to claim 23 wherein said conjugate comprises ~~the detectable molecule is~~ Green Fluorescent Protein.

30. (Withdrawn) A method according to claim 23 wherein the cell is a mammalian cell.

31. (Withdrawn) A method according to claim 23, wherein the cell is selected from the group consisting of bacterial cells, yeast cells, fungal cells, plant cells and animal cells.

32. (Withdrawn) A method according to claim 23, wherein the cell normally expresses a GPCR.

Serial No. 10/628,909

Filing Date: July 29, 2003

33. (Withdrawn) A method according to claim 23, wherein the cell has been transformed to express a GPCR not normally expressed by such a cell.

34. (Withdrawn) A method according to claim 23, where the test compound is in aqueous solution.

35. (Withdrawn) A method according to claim 23, where the cells are deposited on a substrate.

36. (Withdrawn – currently amended) A method of screening a sample solution for the presence of an agonist to a G protein coupled receptor (GPCR); comprising: a) providing a cell expressing a GPCR and containing a conjugate according to claim 1; ~~the conjugate comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the cell to a sample solution; and then c) detecting translocation of said conjugate ~~the detectable molecule~~ from the cytosol of the cell to the membrane edge of the cell; wherein movement of said conjugate ~~the detectable molecule~~ from the cytosol to the membrane edge of the cell after exposure of the cell to the sample solution indicates the sample solution contains an agonist for a GPCR expressed in the cell.

37. (Withdrawn) A method according to claim 36 wherein the cell expresses a known GPCR.

38. (Withdrawn) A method according to claim 36 wherein the cell expresses an unknown GPCR.

39. (Withdrawn) A method according to claim 36 wherein the cell expresses an odorant GPCR.

40. (Withdrawn) A method according to claim 36 wherein the cell expresses a  $\beta$ -adrenergic GPCR.

41. (Withdrawn – currently amended) A method according to claim 36 wherein said conjugate ~~the detectable molecule~~ is optically detectable.

42. (Withdrawn – currently amended) A method according to claim 36 wherein said conjugate comprises ~~the detectable molecule~~ is Green Fluorescent Protein.

43. (Withdrawn) A method according to claim 36 wherein the cell is a mammalian cell.

44. (Withdrawn) A method according to claim 36, wherein the cell is selected from the group consisting of bacterial cells, yeast cells, fungal cells, plant cells and animal cells.

Serial No. 10/628,909

Filing Date: July 29, 2003

45. (Withdrawn – currently amended) A method of screening a test compound for G protein coupled receptor (GPCR) antagonist activity, comprising: a) providing a cell expressing a GPCR, and containing a conjugate according to claim 1; ~~the conjugate comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the cell to a test compound; c) exposing the cell to a GPCR agonist; and d) detecting translocation of said conjugate ~~the detectable molecule~~ from the cytosol of the cell to the membrane edge of the cell; where exposure to the agonist occurs at the same time as, or subsequent to, exposure to the test compound, and wherein movement of said conjugate ~~the detectable molecule~~ from the cytosol to the membrane edge of the cell after exposure of the cell to the test compound indicates that the test compound is not a GPCR antagonist.

46. (Withdrawn) A method according to claim 45 wherein the cell expresses a known GPCR.

47. (Withdrawn) A method according to claim 45 wherein the cell expresses an odorant GPCR.

48. (Withdrawn) A method according to claim 45 wherein the cell expresses a  $\beta$ -adrenergic GPCR.

49. (Withdrawn – currently amended) A method according to claim 45 wherein said conjugate ~~the detectable molecule~~ is optically detectable.

50. (Withdrawn – currently amended) A method according to claim 45 wherein said conjugate ~~comprises the detectable molecule~~ is Green Fluorescent Protein.

51. (Withdrawn) A method according to claim 45 wherein the cell is a mammalian cell.

52. (Withdrawn) A method according to claim 45, wherein the cell is selected from the group consisting of bacterial cells, yeast cells, fungal cells, plant cells and animal cells.

53. (Withdrawn) A method according to claim 45, where the cells are deposited on a substrate.

54. (Withdrawn – currently amended) A method of screening a test compound for G protein coupled receptor (GPCR) antagonist activity; comprising: a) providing a cell expressing a GPCR and containing a conjugate according to claim 1; ~~the conjugate comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the cell to a GPCR agonist so that translocation of the detectable molecule from the cytosol of the cell to the membrane edge of the cell occurs; c) exposing the cell to a test compound; where exposure to the agonist occurs prior to exposure to the test compound, and wherein movement of said

Serial No. 10/628,909

Filing Date: July 29, 2003

~~conjugate the detectable molecule~~ from the membrane edge of the cell to the cytosol after exposure of the cell to the test compound indicates that the test compound has a GPCR antagonist activity.

55. (Withdrawn – currently amended) A method according to claim 54 wherein said conjugate the ~~detectable molecule~~ is optically detectable.

56. (Withdrawn – currently amended) A method according to claim 54 wherein said conjugate comprises the ~~detectable molecule~~ is Green Fluorescent Protein.

57. (Withdrawn) A method according to claim 54 wherein the cell is a mammalian cell.

58. (Withdrawn) A method according to claim 54, wherein the cell is selected from the group consisting of bacterial cells, yeast cells, fungal cells, plant cells and animal cells.

59. (Withdrawn) A method according to claim 54, where the test compound is in aqueous solution.

60. (Withdrawn) A method according to claim 54, where the cells are deposited on a substrate.

61. (Withdrawn – currently amended) A method of screening a cell for the presence of a G protein coupled receptor (GPCR); comprising: a) providing a test cell, said test cell containing a conjugate according to claim 1; ~~comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the test cell to a solution containing a GPCR agonist; and c) detecting translocation of said conjugate the ~~detectable molecule~~ from the cytosol of the cell to the membrane edge of the cell; wherein movement of said conjugate the ~~detectable molecule~~ from the cytosol to the membrane edge of the test cell after exposure of the test cell to the GPCR agonist indicates that the test cell contains a GPCR.

62. (Withdrawn – currently amended) A method according to claim 61 wherein said conjugate the ~~detectable molecule~~ is optically detectable.

63. (Withdrawn – currently amended) A method according to claim 61 wherein said conjugate the ~~detectable molecule~~ is Green Fluorescent Protein.

64. (Withdrawn) A method of screening a plurality of cells for those cells which contain a G protein coupled receptor (GPCR); comprising: a) providing a plurality of test cells, said test cells containing a conjugate according to claim 1; ~~comprising a  $\beta$ -arrestin protein and a visually detectable molecule~~; b) exposing the test cells to a known GPCR agonist; and c) detecting those cells in which said conjugate the

Serial No. 10/628,909

Filing Date: July 29, 2003

~~detectable molecule~~ is translocated from the cytosol of the cell to the membrane edge of the cell; wherein movement of said conjugate ~~the detectable molecule~~ from the cytosol to the membrane edge of a cell after exposure to the GPCR agonist indicates that the cell contains a GPCR for that known GPCR agonist.

65. (Withdrawn – currently amended) A method according to claim 64 wherein said conjugate ~~the detectable molecule~~ is optically detectable.

66. (Withdrawn – currently amended) A method according to claim 64 wherein said conjugate comprises ~~the detectable molecule~~ is Green Fluorescent Protein.

67. (Withdrawn) A method according to claim 64 wherein the plurality of test cells are contained in a tissue.

68. (Withdrawn) A method according to claim 64 wherein, the plurality of test cells are contained in an organ.

69. (Withdrawn) A method according to claim 64 wherein step (b) comprises exposing the test cells to a plurality of known GPCR agonists.

70. (Withdrawn) A substrate having deposited thereon a plurality of cells, said cells expressing a GPCR and containing a conjugate, the conjugate comprising a  $\beta$ -arrestin protein and a detectable molecule.

71. (Withdrawn) A substrate according to claim 70, wherein the detectable molecule is an optically detectable molecule.

72. (Withdrawn) A substrate according to claim 70, wherein the detectable molecule is Green Fluorescent Protein.

73. (Withdrawn) A substrate according to claim 70 wherein the cell is a mammalian cell.

74. (Withdrawn) A substrate according to claim 70, wherein the cell is selected from the group consisting of bacterial cells, yeast cells, fungal cells, plant cells and animal cells.

75. (Withdrawn) A substrate according to claim 70, wherein the cell expresses an olfactory GPCR.

76. (Withdrawn) A substrate according to claim 70, wherein the cell expresses a  $\beta$ -adrenergic GPCR.

Serial No. 10/628,909

Filing Date: July 29, 2003

77. (Withdrawn) A substrate according to claim 70, wherein the substrate is made of a material selected from glass, plastic, ceramic, semiconductor, silica, fiber optic, diamond, biocompatible monomer, and biocompatible polymer materials.

78 – 83 . (Cancelled)

84. (New) The conjugate according to claim 1, wherein said label is a fluorescent label.

85. (New) The conjugate according to claim 1, wherein said label is a colorimetric label.

86. (New) The conjugate according to claim 1, wherein said label is a radioactive label.

87. (New) The conjugate according to claim 1, wherein said label is an electron-dense label.